VISUAL INFORMATION TRANSFER IN ALBINO RATS AS MEASURED WITH MICROELECTRODE RECORDING TECHNIQUES

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VISUAL INFORMATION TRANSFER IN ALBINO RATS AS MEASURED WITH MICROELECTRODE RECORDING TECHNIQUES

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CHAPTER I

INTRODUCTION

Albino rats develop severe retinal degeneration following exposure to continuous illumination. Despite a complete loss of photoreceptor cells of the retina, behavioral experiments confirm that these animals retain functional vision. The transfer of visual information from the retina to the central nervous system in animals lacking receptor cells has not been established. While such a conclusion may reasonably be inferred on the basis of the behavioral work, evoked activity recorded from single neurons within the visual system of animals whose retinas lack photoreceptor cells would be necessary to establish functional vision. Utilizing electrophysiological methods the present study was designed to assess the status of single neurons within the visual system of normal retinal rats and more importantly, in rats whose retinas were devoid of photoreceptor cells.

Microelectrode recording techniques and histogram analysis methods were used to compare the response properties of neurons in the visual system of normal retina rats and rats with extensive retinal damage to visual stimulation. A schema for the classification of lateral geniculate

nuclei (LGN) cells from animals with intact retinas was developed according to the distinctive features of the response pattern histograms. The LGN cells from the control animals were divided into three categories: SIMPLE-ON; SIMPLE-OFF; and COMPLEX. More importantly, visual signals transferring from the retina to the central nervous system in degenerate retina animals was recorded. However, all of the LGN cells recorded from the experimental animals with retinal damage displayed response patterns that were characteristic of the normal COMPLEX cell type. The reasons for such differences between animal groups were left for later experimentors to determine.

A detailed explanation of the Visual Pathways; Receptive Fields; Retinal Degeneration; Behavioral and Neurophysiological Indices; and a Proposed Model for the Lateral Geniculate Nucleus can be found in Chapter 2. Chapter 3, Methods and Procedures details the recording procedures, the stimulation techniques and the data analysis and acquisition techniques. Examples of the response patterns of each cell type are presented in Chapter 4, Results. Finally, an overview of the response patterns is presented in Chapter 5, Discussion.

CHAPTER II

LITERATURE REVIEW

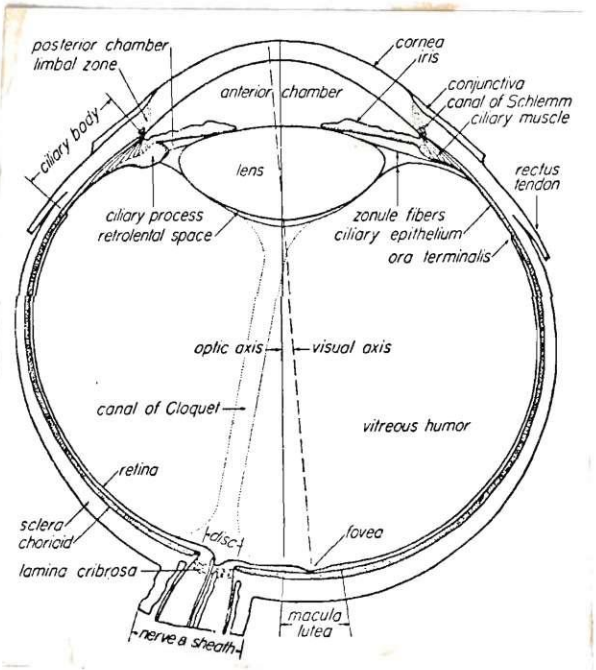
Visual Pathways

The nervous layer of the eye (see Fig 1) is the retina. The retina is a complex, ten-layered structure (see Fig 2) derived embryologically from the central nervous system. In mammals, the major neural components of the retina consist of the photoreceptor cells, the bipolar cells, and the ganglion cells. The receptor cells of the retina, cone shaped and rod shaped, are located nearest the chorioid. The basal portions of the receptor cells establish synaptic connections with the processes of the bipolar cells. The bipolar cells, in turn, synapse with the ganglion cells. Subsequently, the axons of the ganglion cells converge to form the optic nerve and pierce the chorioid and scleral coats of the eyeball. In addition, the retina contains numerous horizontal and amacrine cells that serve as interneurons to integrate retinal functions. Finally, a supportive element of the retina, the Müller cells, furnish glucose to the nerve cells and are able to synthesize and store glycogen.

Within the primate visual system each optic nerve enters the cranial acvity and converges at the optic chiasm.

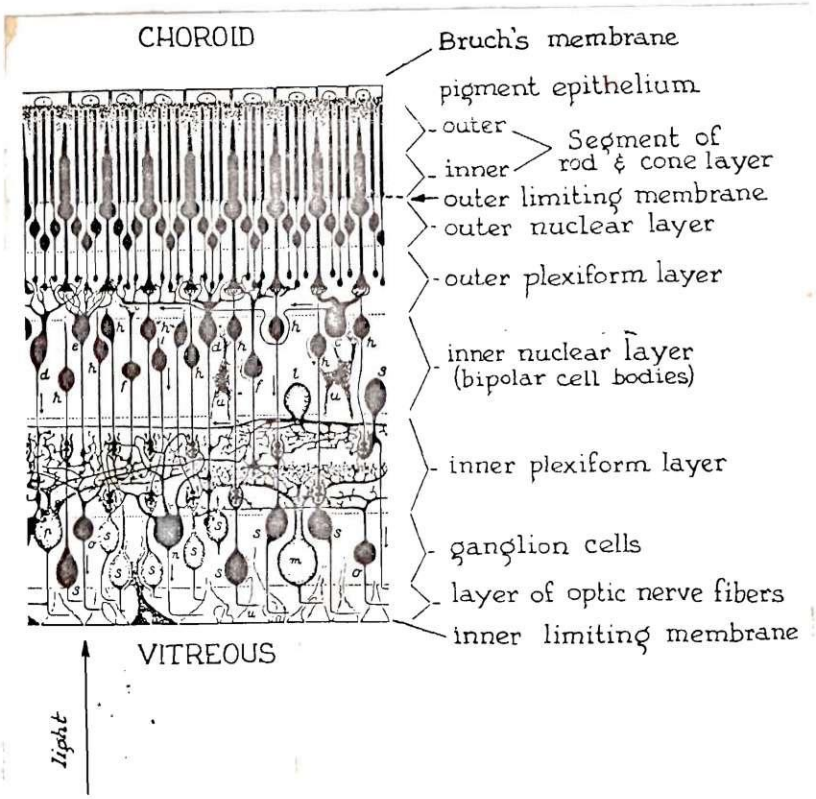
Here, the fibers from the nasal side of each retina decussate and enter the contralateral optic tract, while the fibers from the temporal half of each retina continue into the ipsalateral optic tract. Thus, each optic tract contains fibers originating from the ipsalateral temporal retina and the contralateral nasal retina. Fibers from each optic tract terminate in the ipsalateral thalamus. The specific thalamic relay nucleus for the visual pathway is the lateral geniculate body. Some optic tract fibers terminate in the pretectal nuclei and the superior colliculi. The latter two nuclear zones are believed to be involved in pupillary reflexes and the control of eye movements. Projection cells in the lateral geniculate nuclei give rise to the optic radiation (or geniculo-calcarine tract), which projects to the primary visual cortex located in the occipital lobe. Visual information also reaches the visual association cortex, which surrounds the primary visual area. The rat visual system is believed to be similar to the primate visual system, although the anatomical connections have not been as extensively studied.

There are at least two major neuronal pathways within the retina by which visual information can be transmitted to the central nervous system. In mammals, one pathway containing few neurons, allows for rapid transmission of information through the retina to the central nervous



Horizontal section of the primate eye showing rays of light being focused upon the retina. (Fig 1 from Wall, The Vertebrate Eye, Bloomfield Hills, Mich., Cranbrook Inst. of Science; for further reference see Ruch and Patton, Physiology and Biophysics, pg. 401, 1966).

Figure 1. Physical Structure of the Eye



Functional anatomy of the retina based on a Golgi impregnation stain. The principal cell types and their synaptic relations are shown. Various cell types include:

c: horizontal cells
d, e, f: diffuse bipolar cells
m, n, o, p, r, s: ganglion cells

(Fig 2 from Polyak, The Retina, Chicago, University of Chicago Press; for further reference see Ruch and Patton, Physiology and Biophysics, pg. 423, 1966).

Figure 2. Structure of the Retina

system. The pathway from one photoreceptor cell to one bipolar cell, to one ganglion cell allows a minimal amount of interaction of information within the retina. A second indirect pathway is marked by a convergence of many receptors onto bipolar cells and of many bipolar cells upon ganglion cells. Convergence is a neural substrate for an interaction of streams of impulses that result in facilitation and inhibition phenomena. This arrangement affords a basis for the receptors of a retinal region to interact at the bipolar and ganglion cell level. Slower transmission and greater modification of information characterize the indirect pathway. Interaction is further facilitated by a system of intraretinal associative neurons, the horizontal and amacrine cells.

Receptive Fields

The receptive field of a retinal ganglion cell is defined as the portion of the visual field from which the discharge of the ganglion cell can be increased or decreased (Hartline, 1938; Kuffler, 1953). By focusing a fine beam of light on the retina, the areas of the retina that excite, or inhibit each neuron can be determined. Retinal ganglion cells of the mammalian eye also conduct action potentials when the retina is exposed to no light at all. The response to light of a particular ganglion cell may follow three basic patterns. Certain cells

respond to the onset of the light stimulus ("on response"). Other cells, if responding prior to the stimulus, cease to fire following the onset and resume firing at the cessation of the light stimulus ("off response"). A third type of fiber behavior, is characterized by firing at the onset and at the cessation of the light stimulus ("on-off response").

In 1953, Kuffler discovered that the receptive fields of retinal ganglion cells had an annular organization in which the center and the periphery were mutually antagonistic. In some cells light stimulation of the center of the receptive field increased the neural discharge rate. In other cells, the center of the receptive field was inhibitory, giving a response only when the light stimulation ceased, while the periphery gave an "on" response during light stimulation. Rodiek and Stone (1965a; 1965b) demonstrated that the intensity of an excitatory or inhibitory response was dependent on the amount of appropriate region stimulated (summation). On the other hand, stimulating an "on" area and an "off" area of a single unit, simultaneously, resulted in a cancellation of the effects (mutual antagonism).

The first receptive field plots for neurons in the visual cortex were made by Hubel and Wiesel (1959; 1961; 1965). The receptive fields were described in terms of their geometrical and functional attributes. The

geometrical and functional parameters of a cell result from the anatomical structure responding to the mapping stimulus. Different characteristics of the stimulus which will cause excitation of the cortical cell may include size, shape, color, orientation, and rate and direction of movement. For example, a direction sensitive unit will show different receptive field "shapes" when mapped with a moving spot dependent on the scanning direction. Units with inhibitory areas, with different relative strengths, will have different resting levels of activity that depend upon the total level of illumination. A complete description of the receptive field properties of a given unit would require a set of mathematical or logical statements defining the output transfer functions over the pertinent parameters.

The organization of the receptive fields of neurons within the lateral geniculate nucleus differs only slightly from patterns established for ganglion cells. Hubel (1962) studied the complex integrative action of the lateral geniculate nucleus from light stimulation of the retina. Responses of the primate lateral geniculate body resembled those found in the primate retinal ganglion cells. The response of a lateral geniculate cell may be an "on" or an "off" or an "on-off" response. The receptive fields of neurons in the lateral geniculate nuclei can be mapped by

discrete light stimuli focused upon the retina. The fields are circular, with a central region bordered by an annular surround. Similar to retinal ganglion cells, the central region may be excitatory and the surrounding region inhibitory, or vice versa.

Poggio, Baker, Lamane and Riva Sanservino (1966) reported that the synaptic chains linking the center of the receptive field to a particular geniculate neuron exert a more powerful effect on the unit than do those which link the surrounding area of the same receptive field to the same geniculate neuron. A measure of interaction between functionally antagonistic regions of the receptive field can be obtained by counting the average number of transient excitatory responses evoked at various times after the onset of stimulation of the inhibitory region and subsequently plotting the responses as a function of the delay between center and surround stimuli. Poggio et al. (1969) demonstrated that inhibition initially increases rapidly and reaches a maximum when the center stimulus is delivered 10-30 msec after the onset of the surround inhibitory stimulus. The inhibitory effect the declined and in most instances the effect falls to one-half of its maximum at delays of 100-200 msec.

The antagonistic organization of the retinal receptive fields, changes during dark adaption (Barlow, Fitzhugh

and Kuffler, 1957). In the dark adapted eye, no antagonism between peripheral and central regions was found. In other words, the spatial responsiveness of the dark-adapted eye was summative in character, whereas the light-adapted eye was characterized by excitatory and inhibitory effects opposing each other in the central and outer regions of the receptive field. Poggio et al. (1969) observed a similar phenomenon at the level of the lateral geniculate. Poggio (1969) and his colleagues further found that the characteristics of retinal organization may be the basis of center surround interactive mechanism in the lateral geniculate nucleus and proposed that the amacrine cell was the integrative element on which the mechanism depended.

Retinal Degeneration

Exposure of adult albino rats to continuous low-intensity (18 ft-c indirect; 70 ft-c direct) light has resulted in degenerative changes in the retina and electrophysiological changes throughout the visual system (Anderson and O'Steen, 1971a; O'Steen and Anderson, 1971a; O'Steen and Lytle, 1971; Bennett, Dyer and Dunn, 1972). Morphological changes consisted of a degeneration of the retina that was selective and experimentally graded. For example, exposure to continuous illumination for 4 days resulted in fragmentation and disorientation of the outer segments of the receptor cells and pyknosis of some nuclei

in the outer nuclear layer in the posterior portion of the retina. Tissue damage in peripheral areas of the retina remained negligible. Exposure for 14 days resulted in a disappearance of the receptor cells in the posterior retina. In the peripheral retinal areas, the receptor cell nuclei and portions of the inner and outer segments unaltered. After 30 days of illumination, all receptor cells in posterior eye had disappeared, while some scattered receptor cell nuclei remained in anterior retina, but were pyknotic (O'Steen, 1970; Anderson and O'Steen, 1971a; Anderson and O'Steen, 1971b; O'Steen and Anderson, 1971a).

The active degeneration of the outer segments of the receptor cells elicited a "phagocytic cell" invasion of the retina. Phagocytic cells, atypical to the retina, were responsible for the removal of cellular debris. These cells invade and occupy the central retinal area of degeneration, between the receptor layer and the pigment epithelial layer, in animals exposed to 4 days of illumination (O'Steen and Lytle, 1971). The origin of the phagocytic cells is not yet clear. However, phagocytic cells apparently come from several cell populations: (a) from mononuclear cells which migrate through the retina from the vitreous cavity; (b) from pigment epithelial cells which separate from Bruch's membrane; and (c) from the blood vascular system (O'Steen and Lytle, 1971; O'Steen and

Karcioglu, 1974). Following 14 days of exposure the phagocytic cells were absent centrally, but were present in peripheral areas, where photoreceptor destruction was still in progress. Extensive degeneration had occurred more centrally and fragmentation had increased in peripheral areas of the retina. After 30 days of illumination, the phagocytic cells were completely absent from the retina, as well as evidence of the photoreceptor cells.

Once retinal degeneration was initiated, further progression of damage required additional light exposure. A return to cyclic light conditions elicited a cessation in degeneration followed by a removal of the cellular debris. Continued light exposure disrupted the bipolar cell connections, although cellular degeneration did not extend into the innermost retinal layers (O'Steen and Lytle, 1971). Synapses between the receptor and bipolar cells were lost, so that involvement of the innermost layer resulted from either transneuronal degeneration or direct light damage.

Retinas of albino rats exposed to very short periods of illumination underwent reversible structural change, which was apparently limited to the pigment epithelial cells and photoreceptor cells (Shear, O'Steen and Anderson, 1973). Certainly, the degeneration between 6 and 12 hours was reversible because control animals exposed to a cyclic light schedule (14 hours of light followed by 10 hours of

darkness) developed no retinal damage. Irreversible damage occurred after approximately 96 hours of constant low intensity illumination. Noell, Walker, Kang and Berman (1966) found exposure to intense (138-185 ft-c) flourescent light for only 24 hours was significant to cause irreversible retinal damage, consisting of pyknosis of the receptor cell nuclei in the outer nuclear layer. Using a similar high intensity light source, Grignolo et al. (1969) substantiated the previous findings. Noell et al. (1966) also exposed albino rats to illumination periods of up to 5 months and observed a destruction of the photoreceptor and pigment epithelial cells. Noell et al. (1966) suggested a reaction product from the damaged receptor cells caused the destruction of the pigment cells. In constrast to the earlier work, O'Steen and Lytle (1971) employed a lower intensity illumination and a lower room and body temperature and failed to observe a destruction of the pigment epithelial cells. Gorn and Kuwabara (1967) reported that a reversal in retinal damage occurred following two days of intense light exposure and 14 days of relative darkness. Exposure for more than 7 days was necessary for irreversible retinal damage. Differences in light source intensity account for differences in the length of period reported for reversible retinal damage.

The severity of photoreceptor damage was shown to be

age dependent (O'Steen, Anderson and Shear, 1974). O'Steen et al. (1974) exposed albino rats from 3 weeks of age to adulthood to flourescent and incandescent illuminance and an elevated environmental temperature known to induce receptor destruction in adult animals. Retinas of 3-week and 4-week old experimental animals were apparently unaffected by light exposure. Retinas of some 5-week and most 6-week old rats displayed fragmentation of outer and inner segments of the receptor cells, and pyknotic receptor nuclei in the central region. Areas of focal damage were more severe in 7-week old rats. All subsequent age groups were characterized by a significant reduction in the average thickness of the outer nuclear layer (location of the receptor cell bodies). Comparison of total retinal thickness measurements in different age groups indicated that light exposure significantly reduced the distance between the inner and outer limiting membrane in only some age groups. Reduction in overall thickness of the retina was an ineffective measurement in grading the amount of retinal degeneration. Photoreceptor destruction paralleled the reduction of the outer nuclear layer, as both became progressively more severe as the rats aged.

Destruction of photoreceptor cells by incandescent light progressed at a slightly reduced rate as compared to that of flourescent light exposure of the same intensity.

The high energy wavelengths of the visible spectrum were primarily responsible for causing light induced retinal degeneration (Anderson, Coyle and O'Steen, 1972). Several characteristic differences in the retinal degeneration resulted from variation in the intensity level of illumination. These include: (a) the rate of degeneration, related directly to the strength of the illumination, (b) the extent of retinal degeneration and involvement of the pigment epithelium, and (c) the pattern of degeneration particularly as related to the site of initial cell destruction (O'Steen and Anderson, 1974). Elevated environmental and body temperature were also influential in increasing the rate of destruction.

Electron micrographs of retinas exposed to 30 days of constant illumination revealed severe structural damage (O'Steen, Shear and Anderson, 1972). The damaged area was specifically localized to the photoreceptor cells, and the retinal layer between the pigment epithelium and the inner nuclear layer was totally absent. The other cell layers were apparently not affected by the light. The structure of the retinas exposed to continuous light for four to six months resembled the structure of the retinas of animals exposed to 30 days of illumination. In some instances, the bipolar cells of the retinas exposed to four to six months of illumination were no longer arranged as a layer of

nuclei separated from the ganglion cell layer by the inner plexiform layer. Instead, the bipolar cells extended through the inner plexiform layer to the ganglion cell layer and appeared to be oriented along existing blood vessels.

Behavioral and Neurophysiological Indices

After exposing albino rats to 30 days of constant light, thereby eliminating the photoreceptor cells, one might expect these animals to be blind. In fact, behavioral experiments with rats exposed to 30 days of low-level illumination did not reveal impairments in visually guided behavior (Anderson and O'Steen, 1972). Animals exposed to cyclic light and animals exposed to 30 days of illumination were trained and tested in a T-maze on black-white discrimination tasks and two pattern discrimination tasks. Rats without receptor cells were not impaired on any of the discrimination tests, but performed at high levels of competence (Anderson and O'Steen, 1972). The rats not only retained a visual habit learned prior to retinal degeneration, but were capable of learning new discrimination tasks at rates indistinquishable from normal animals.

The length of time an animal was exposed to constant light determined whether a performance decrement would be observed on some visually guided tasks (Bennett, Dyer and

Dunn, 1972; Bennett, Dyer and Dunn, 1973). Bennett et. al. (1972) exposed animals to constant light for periods ranging from less than 12 days to more than 120 days. Performance was assessed by measuring the percentage of correct responses to visual targets on a light-dark discrimination task. Rats exposed for less than 90 days performed as well as control animals, while the performance of animals exposed for more than 90 days decreased in proportion to the length of time beyond 90 days of exposure. Anderson and O'Steen (1973) exposed rats to 30 days of illumination and used two measures to assess visual performance: the percentage of correct responses to the visual targets and the time taken to make a choice (latency of response). The latency of response was defined as the time taken by the animal to select one of the two visual discriminda after leaving the start-box. The latency of response was a more sensitive indicator for detecting retinal damage than the percentage of correct responses. For the pattern tasks, Anderson and O'Steen (1973) noted a performance decrement in the response latencies, while on the black-white discrimination tasks, no decrement in either performance measures was observed. These studies indicate the importance of the type of experimental design utilized in testing the behavior of animals. Animals with no apparent photoreceptor cells can still perform on

on certain visually guided tasks, although measures of perceptual performance may vary.

Neurophysiological studies have indicated that several classical indices of visualfunction are altered or disrupted throughout widespread portions of the visual system of animals with damaged retinas. In one series of experiments using macroelectrodes (Anderson and O'Steen, 1971b), the spontaneous rhythmic and nonrhythmic potentials were altered or abolished in animals exposed to continuous light for 30 days. The continuous state of activity which can be recorded throughout the intact visual system is termed spontaneous, as it not aroused by specific visual stimulation. The visual state normally exists in an equilibrium between two outstanding forces. The characteristics of the spontaneous activity recorded from animals with damaged retinas depended upon the duration of light exposure and upon the amount of retinal degeneration (Anderson and O'Steen, 1971a; O'Steen and Anderson, 1971b). Experiments have also indicated that exposure to continuous light produced alterations in the electrical activity recorded from the eye. Electroretinograms were markedly altered in animals exposed to 2 or more days of constant light (Anderson and O'Steen, 1971b).

Spontaneous rhythmic activity potentials falling into 3 distinct frequency ranges were recorded throughout

widespread regions of the rat visual system (Anderson and O'Steen, 1971a). The exact frequency and shape of the rhythmic potentials were found to depend upon the level of anesthesia and the lighting conditions present at the time of recording (Anderson and O'Steen, 1972). The most predominant potential had a frequency of 10-25 cycles/sec., the second potential had a frequency od 100-150 cycles/sec., and the third potential had a frequency of 0.3-0.5 cycles/sec. Since the rhythmic potentials were absent in enucleated animals and in animals with experimentally induced retinal degeneration, it was concluded that the potentials were of retinal origin (Anderson and O'Steen, 1971a; Anderson and O'Steen, 1971b). No changes in rhythmic activity resulted from changes in ambient light levels, although flashes of light disrupted the activity during the periods of evoked response. The receptor cells were suspected of functioning to trigger-off the rhythmic activity that was actually generated in other retinal layers. Evidence from intra-retinal recording of the bullfrog by Tomita and Funaihi (1952) and the frog by Brindley (1956), revealed oscillatory potentials that were greatest in the region of the bipolar cells. These experiments indicated that the bipolar cell may give rise to the oscillatory potentials, but were insufficient to independently generate the potentials. The production of rhythmic potentials from

bipolar cells, consequently depended upon the activity of receptor cells in the presence of other cell layers of the retina.

Exposure of 4 days of continuous light resulted in either an absence of rhythmic potentials in the rat visual system or potentials that were only vaguely similar to potentials found in rats with normal retinas. Animals exposed to 14 days of low intensity illumination exhibited a lack of recordable oscillatory potentials throughout the visual system. Recording from the optic tract, lateral geniculate nucleus and the visual cortex revealed a complete absence of all three kinds of rhythmic potentials found in control rats (Anderson and O'Steen, 1972). Following 30 days of exposure to continuous low intensity illumination, the rhythmic potentials were absent throughout widespread regions of the visual system (Anderson and O'Steen, 1971b).

Neurophysiological experimentation has not yet established that neurons in the central nervous system of retinal damaged animals respond to visual stimulation. The present study utilizes electrophysiological methods to assess the functional status of single neurons within the visual system of normal rats and rats exposed to more than 30 days of continuous low intensity illumination. More specifically, the present study will utilize microelectrode

recording techniques and computer analysis methods to compare the response properties of neurons in the lateral geniculate nucleus of normal animals with the response properties of neurons in the lateral geniculate nucleus of animals with extensive retinal damage. Such comparisons should help in understanding the functional differences between normal visual system and the visual system that has been severely damaged.

Proposed Model for the Lateral Geniculate Nucleus

A neuronal model for the organization of the rat lateral geniculate nucleus was proposed by Burke and Sefton (1966a; 1966b; 1966c). The evidence presented by Burke and Sefton (1966a) suggests the existence of two types of lateral geniculate nuclei (LGN) cells: P-cells (principal cells) which project to the visual cortex; and I-cells (interneurons). The I-cell burst pattern is similar to the burst pattern recorded from the interneuronal Renshaw cell and the inhibitory interneurons of the cerebellum. Additionally, in response to optic nerve stimulation, the I-cells respond with longer repetitive discharges, and exhibit a lower threshold and longer latency of response than the P-cells. A waveform characteristic of antidromic invasion is present in most P-cells tested by stimulation of the visual cortex. The antidromic waves of the cat lateral

geniculate nucleus were identified by Bishop, Burke and Davis (1962). The synaptic potentials identified on orthodromic response were not present with antidromic invasion.

In the simple neuronal model incoming optic tract impulses excite P-cells which, through their collaterals excite I-cells. The I-cell discharges, inhibit P-cells. With cessation of I-cell discharges, the P-cell wanes and as individual P-cells recover they discharge in a short burst. The I-cells are reactivated and P-cells are further inhibited. A small amount of presynaptic inhibition can be induced from the visual cortex, although the major portion of inhibitory influences in the model are post-synaptic. Burke and Sefton (1966b) reported that the major evidence for a post-synaptic inhibition came from the correlation between the phase of the inhibition and the period of hyperpolarization of the P-cells. Additionally, neither the inhibition nor the recurrent discharges of the P-cells and the I-cells are affected by removal of the visual cortex, indicating that the inhibition is probably generated within the lateral geniculate body.

If the degree of inhibition of P-cells depends on the temporal summation of the hyperpolarization produced by I-cells, the asynchrony in the discharges of I-cells should reduce the inhibition and more P-cells would fire to a second stimulus. Sefton and Burke (1966) reported

that continued optic nerve stimulation did produce an increase in the number of P-cells discharging to further stimuli. However, the I-cells could not be re-excited from optic nerve stimulation. Thus, it appears that asynchrony in the discharges of I-cells, increased the number of P-cells that could discharge.

Studying the response of P-cells of the rat lateral geniculate body to single shock stimulation of the optic tract, Fukada (1973) found that P-cells could be subdivided into two groups, fast and slow cells according to their initial spike latencies. The two groups also differed in other characteristics of the response to optic tract stimulation. The fast cells also exhibited shorter latency periods for their discharge of activity. Fukada et al. (1973) suggested that the fast cells might receive a less sustained action from the inhibitory interneurons (I-cells) than the slow cells.

The fact that early discharges of fast cells have shorter latencies than those of slow P-cells cannot be explained in terms of their conduction time through the optic nerve fibers, since they are less than 10 msec (Sumitomo, Iwana, and Arikuni, 1969). The suggestion that the ganglion cell of the retina can be differentiated with respect to rapidity of the response to flash stimulation received support from the cat retina ganglion cell (Cle-

land, Dubin and Levick, 1971). In the rat retina, Brown and Rojas (1965a; 1965b) reported that two groups of ganglion cells exist which have different visual response characteristics and have different types of intra-retinal connections.

CHAPTER III

METHODS AND PROCEDURES

Rationale

The overall rationale for the electrophysiological procedures that were used in this research, was to analyze responses of the lateral geniculate nuclei (LGN) neurons to visual stimulation. The goal was to obtain an understanding of the visual information transfer at the level of the single cell. The particular sequence of procedures used in this research allowed for an efficient collection of data from the normal intact retina animals. A schema for the classification of LGN cells from the normal data was developed and used for a comparison of response patterns generated from the LGN cells of animals with degenerative retinas.

General Procedures

Preparation

Adult albino female rats weighing 180-380 grams were maintained in an environment of constant or cyclic light (see Table 1). Animals were from inbred stock and were of the Spraque-Dawley strain of rats. The animals in the cyclic-light group (n=17) were exposed to 14 hours of light and 10 hours of darkness in each 24 hour period.

The animals in the constant-light group (n=6) were exposed to continuous light for periods ranging from 45 to 150 days. During the experimental period all animals were unanesthetized and unrestrained in their cages. The constant light environment had an illumination of 18 ft-c measured as reflected light from the cage floor and 70 ft-c as measured from outside of the cage; light was fom two GE (F15T8.CW) 15-W flourescent tubes (waves of 3800-7500 Å and peaking at 6000 Å), located 40 cm from the top of the animal's cage. Throughout the experiment room temperature was 25 $\pm$ 1° C and food and water were provided ad libitum.

Surgery

All rats were anesthetized with pentobarbital sodium (35 mg/kg body weight, i.p.) prior to surgery. The rats were restrained in a Kopf, small-animal stereotaxic apparatus (see Fig 3). The EKG was monitored on a Tektronix 561A oscilloscope and an audio sound system. Body temperature was maintained by placing the animal on a Gorman-Rupp, constant temperature heating pad. Prior to recording, the cranial skin was incised and the calvarium and dura overlying the optic tract, lateral geniculate nuclei and visual cortex were removed. The pupils were dilated with 1% atropine sulfate. The physiological condition of the animal was continuously monitored during surgery and throughout the recording session by examining

Table 1. Experimental Animals

Animal Number	Weight (approx. gms)	Age (wks)	Retinal Condition	Exposure Times (wks)
1	180	13	normal	cyclic
2	200	14	normal	cyclic
3	240	14	normal	cyclic
4	245	15	normal	cyclic
5	260	15	normal	cyclic
6	260	16	normal	cyclic
7	245	16	normal	cyclic
8	275	16	normal	cyclic
9	280	18	normal	cyclic
10	300	19	normal	cyclic
11	335	20	degenerate	6
12	170	7	normal	cyclic
13	185	8	normal	cyclic
14	180	8	normal	cyclic
15	205	10	normal	cyclic
16	220	11	normal	cyclic
17	235	12	normal	cyclic
18	360	26	degenerate	15
19	240	13	normal	cyclic
20	370	27	degenerate	16
21	385	28	degenerate	17
22	375	30	degenerate	18
23	390	31	degenerate	20

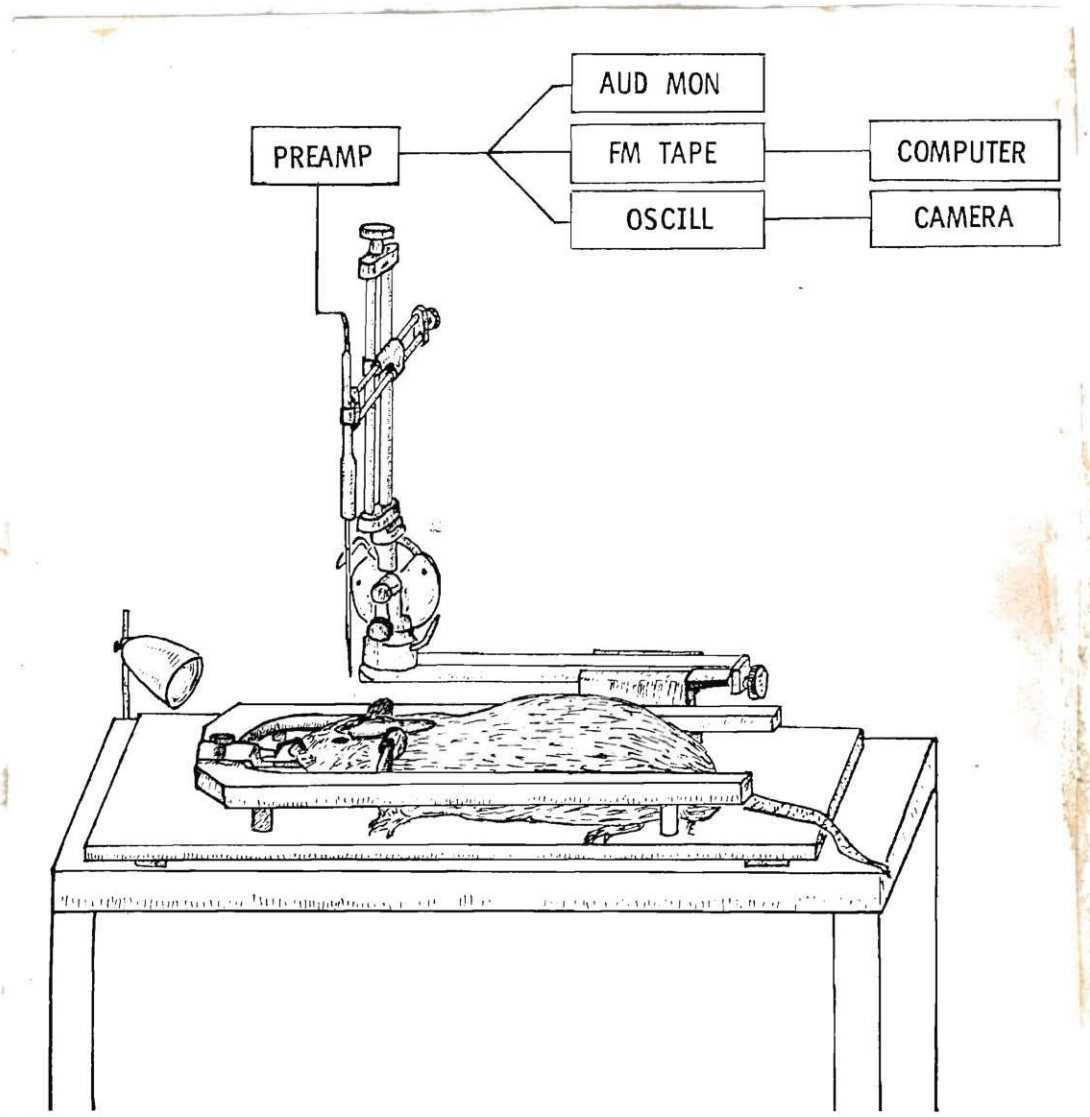


Figure 3. Experimental Set-Up

several physiological parameters. For example, a sharp increase or slow decrease in heart rate indicated that the animal might be experiencing breathing vomplications. Increased salivation and constriction of cortical surface vessels characterized a deterioration in the animal's condition.

Electrodes

Microelectrodes used in the experiments were glass capillary tubes pulled to a tip diameter of 1.5 to 3 micra and filled with 2M NaCl. Electrode coordinates for recording in the lateral geniculate nucleus were derived from the DeGroot stereotaxic atlas. The rat's head was placed in a fixed position such that the interaural line (an imaginary line that passes through the center of each plug when the rat is placed in the stereotaxic instrument) was exactly five millimeters below the level of the upper incisor bar. In the coordinate system of DeGroot (1959) the horizontal zero plane is tangent to the upper incisor bar and 5.0 mm above the interaural line. It passes through the anterior and posterior commissures. The dorsal-ventral coordinates are indicated by a plus measurement above "0" and a minus measurement below "0" (the horizontal zero plane). The rostral-caudal or anterior-posterior coordinate is preceeded by a minus (-) sign in those sections which are posterior to the vertical zero plane and by a

positive (+) sign for those sections anterior to the vertical zero plane. The medial-lateral coordinate is measured as positive value lateral to the midline.

Stimulation Techniques

The photic stimulation used in this experiment were a flash stimulus, a constant light stimulus and a concurrent flash and constant light stimulus. The recording room was kept in total darkness so as not to present any extraneous visual stimulation. Light flashes with a 10 microsecond duration were derived from a Grass Model PS-2 photic stimulator (intensity range = 9.4×10^4 to 15×10^5 candlepower) and were presented at a rate of one every 5 seconds at a distance of 60 cm from the animal. A constant light stimulus was produced from a Castle Surgical Lamp, Type M46 (120v 1 amp, 60 cycles, 90-110 candlepower). This light source was placed at a distance of 80 cm from the animal. Electrical stimuli to the visual cortex consisted of unidirectional rectangular pulses generated by a Grass Model S-4 stimulator and was delivered to the animal through a Grass Model SIU-5 stimulus isolation unit. The electrical pulses had a duration of 0.1 msec and ranged from 1-50 volts in intensity. This source of stimulation aided in verifying the type of unit under study, since many cells of the lateral geniculate nucleus respond to antidromic invasion following stimulation of the visual cortex.

Data Analysis

Response latencies were computed directly from the oscilloscope or from photographs of responses. Unit responses were analyzed using post-stimulus time histograms and interspike interval histograms.

The Post-Stimulus Time Histogram (PST) program is a product of the Digital Equipment Corporation Program Library. The program records all signals (action potentials) crossing a pre-set voltage threshold level (set at ± 7 microvolts in the present study) following a trigger event (see Fig 4, "NEURONAL ACTIVITY" for example of threshold level). After the primary event (e.g., a stimulus) the program measures the time of occurrence of all subsequent events (neuronal responses) above the threshold level. The PST Histogram represents a sum of all activity following consecutive stimuli (see Fig 4). For one stimulus, the resulting PST histogram can be referred to as a one-epoch PST. For each action potential that occurs following stimulation, the appropriate bin corresponding to the potential's time of occurrence is incremented (see Fig 4, "1 Epoch PST"). Following the second stimulus, the resulting PST histogram can be referred to as a summated two-epoch PST. Two individual, one-epoch PST histograms are summated (see Fig 4, "Summated 2 Epochs"). In actuality 100-epoch PST histograms are used, that is a light

flash stimulus is presented 100 times at 5 second intervals of time. Thus, the program accumulates the time of occurrence for all corresponding neuronal responses. The histograms illustrate the frequency of occurence of action potentials (events) at any time T following stimulation.

In the PST Histogram the stimulus, time-locked axis (abscissa) is segmented into bins and the ordinate value of each bin is equal to the total number of neuronal discharges in the time interval of the bin. The program allows the user to specify the number of times, stimuli and succeeding action potentials will be accummulated (epochs), the duration of the time axis (number of bins), and the resolution of the time axis (bin width).

In addition to recording the time occurrence of events following a stimulus, the PST program can show a zero order histogram. This is a graph revealing the number of action potentials (spike above threshold) following succeeding stimuli (see Fig 4, "1 Epoch zero order"). The abscissa is divided into units of epochs (the number of samples) while the ordinate value of each epoch is proportional to the total number of neuronal discharges which occurred during that sample. This feature of the PST program allows the user to see if the overall activity following consecutive stimuli remains constant through time, or increases or decreases perhaps

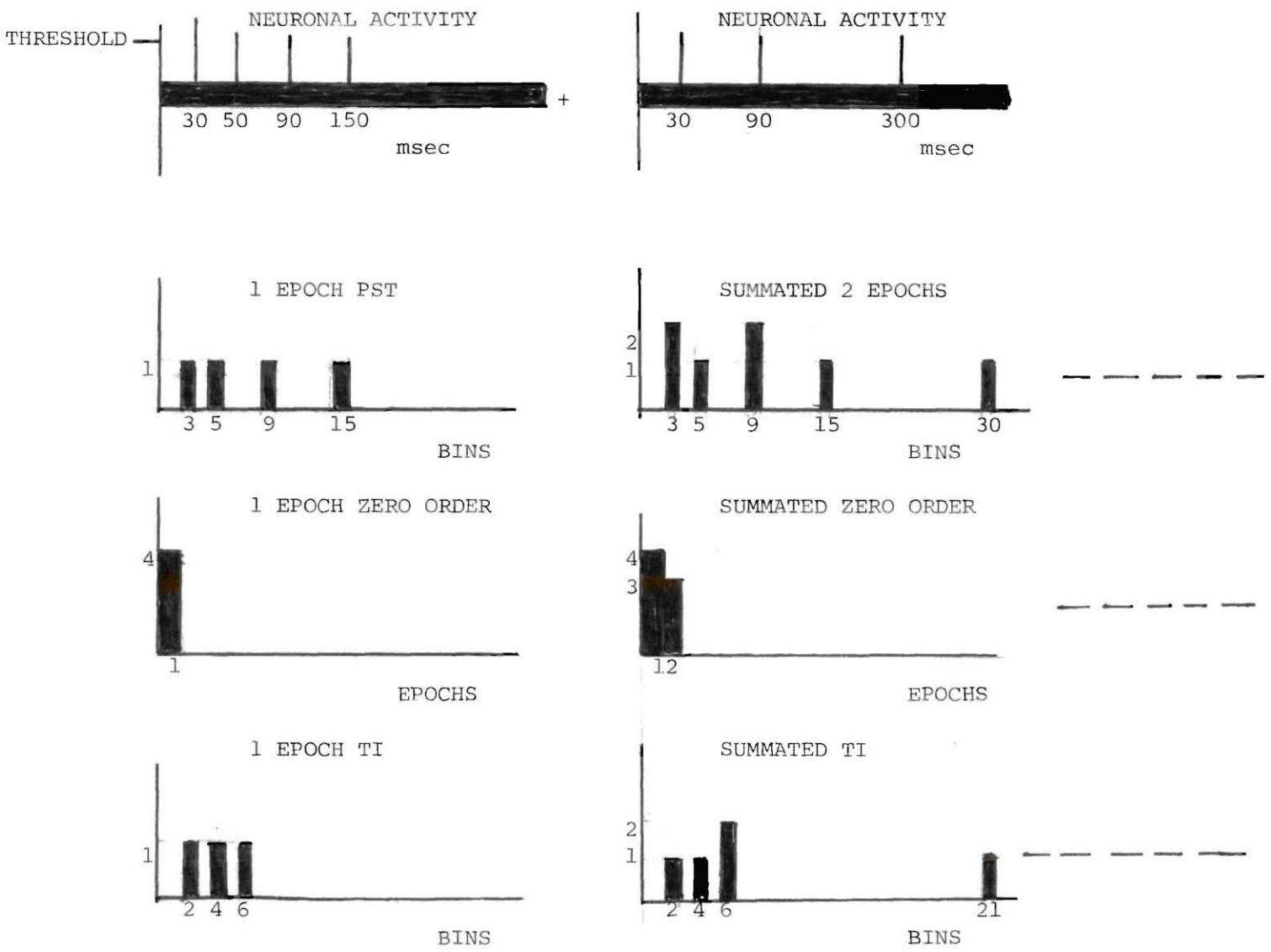


Figure 4. Example of Summating Activity Generating PST and TI Histograms

due to adaption, fatique, or loss of unit (see Fig 4, "Summated zero order").

The Time Interval Histogram (TI) program, also from the DECUS Program Library, measures the frequency of signals which cross a set threshold level. The program stores these signals (action potentials) as a function of the time intervals between them. For one stimulus, the resulting TI can be referred to as a one epoch TI. The time intervals between succeeding action potentials are measured and each bin (time axis) corresponding to the interval of time is incremented (see Fig 4, "1 Epoch TI" and "Summated TI"). The Time Interval Histogram represents a distribution over time of the collected data and the rate at which the data occurred. The data is presented as a plot of frequency of events versus interval time.

Prior to data collection the program allows the user to specify the duration of the time axis (number of bins), the resolution of the time axis (bin width), the minimum time that must pass before an interval is considered a valid interval (mintime), and the total run time of the experiment (epochs).

The Time Interval Histogram allows the user to view the rhythmicity of an incoming signal. For example, a nerve cell firing at exactly one per second will produce a Time Interval Histogram was only one bin incremented. The

program was used as an option to view the spontaneous activity of a single cell in conjunction with the PST Histogram.

Data Acquisition

All neuronal responses were recorded through a Grass High Impedance Probe, Model HIP511C, and fed through a Grass P511 preamplifier to a Tektronix 549 storage oscilloscope for direct visualization. In addition, an audio monitor was used to aid in the detection of single neural units. When a unit responded to a visual stimulus, responses were relayed to a PDP-8L computer for analysis. The results were visualized on a Tektronix RM 503 oscilloscope that is associated with the computer (see Fig 3). Responses were photographed with a Polaroid camera directly from the face of the storage oscilloscope or from the oscilloscope associated with the computer. The experimental procedures used for analysis is detailed in Figure 5. All neuronal units were initially tested for a response to a flash of light. Following the appearence of a visually evoked response, the PST Paradigm was begun. The response patterns generated by flash stimuli during increased ambient illumination and only constant light stimulation were produced according to the PST Paradigm. Data for each histogram was generated by examining the responses of a LGN cell to one-hundred (epochs = 100) consecutive photic stimuli

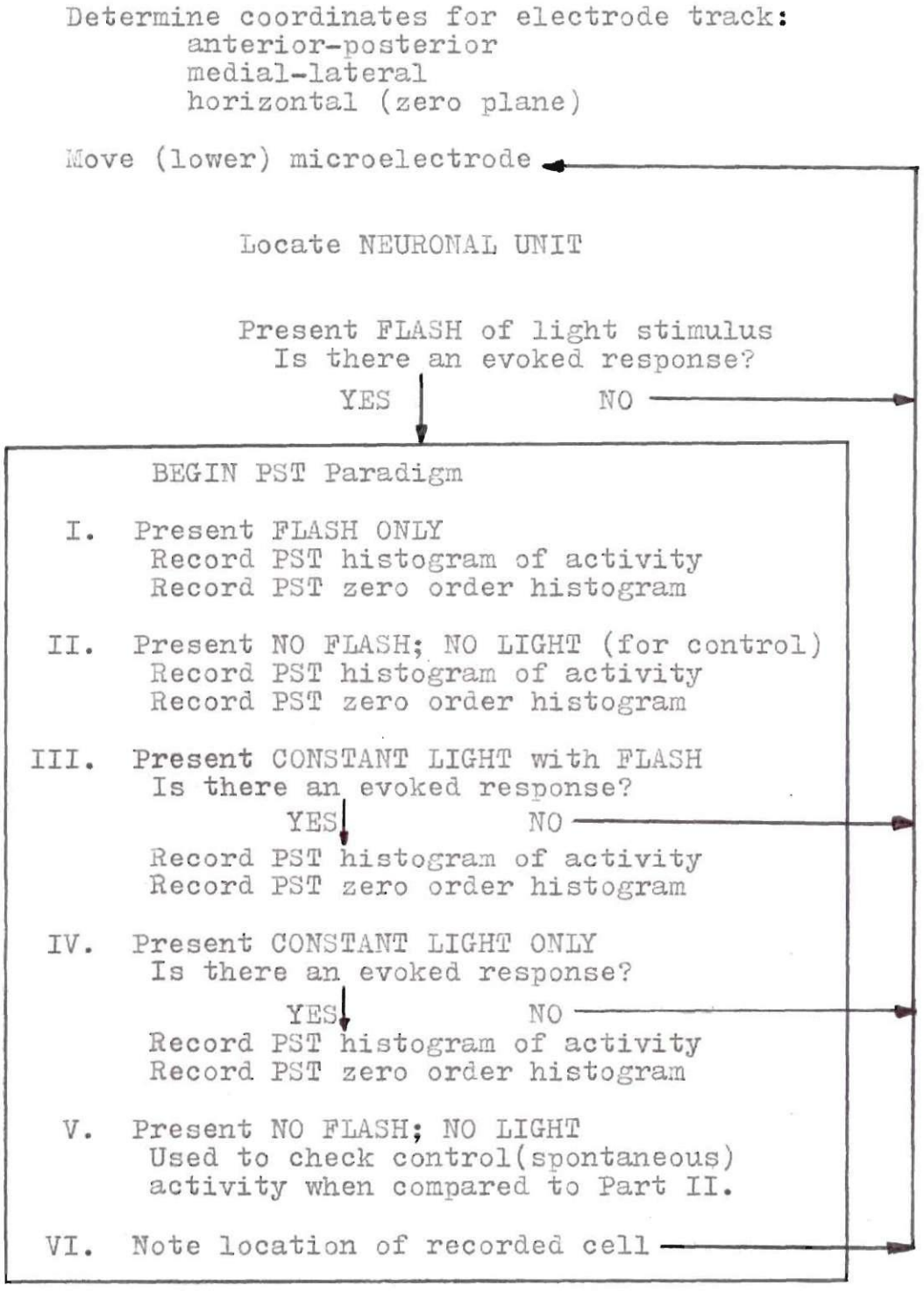


Figure 5. Experimental Procedures

presented to the contralateral retina. Each PST histogram consisted of 100 BINS, 10 msec induration. Each TI histogram consisted of 100 BINS, two msec between each bin.

Electrode Placements

All electrode placements were verified by making D.C. lesions (20 microamps of radio frequency current for 3 minutes) at the site of neural units, after recording response patterns. In addition, D.C. lesions were placed at the deepest penetration of each electrode track to further aid in the histological determination of electrode placement. All lesions were made using a Electronics Life Sciences, Inc., Constant Current Source, Model Number TCCS1A.

Tissue Examination

At the conclusion of each recording session, the eyes were removed and fixed in Bouin's solution for four hours and then placed in 80% alcohol. The brain was placed in 10% buffered formalin for 2-3 weeks. A block of the posterior two-thirds of the left hemisphere was removed for histological confirmation of electrode placement. The tissue can then be processed routinely and stained in either hemotoxylin-eosin or cresylecht violet for tissue examination.

Facilities Available

Laboratory

This research was performed in the laboratory of Dr. K. V. Anderson. The laboratory included an electrophysiology lab, a histology lab and a dark room.

Animals

All animals were housed at the animal quarters at Emory University in the Department of Anatomy.

CHAPTER IV

RESULTS

A classification schema was developed for neurons in the lateral geniculate nuclei (LGN) of rat's with normal intact visual systems. This classification of cells was based according to the response patterns generated by flash stimulation to the contralateral retina. A detailed understanding of this classification system will be fully developed in this chapter, concurrent with examples of response patterns of each type. The cell types include:

I. Simple Neurons
   SIMPLE-ON: these neurons display a single wave of increased excitability 20-30 msec (short latency) following flash stimulation

   SIMPLE-OFF: these neurons display a single wave of decreased excitability 30-100 msec following flash stimulation

II. Complex Neurons
   COMPLEX: these neurons are characterized by several waves of increased excitability and one or more waves of decreased excitability produced by flash stimulus

Using this classification scheme developed from the normal data, the response patterns of neurons of the LGN of the degenerate retinal animals were studied. Any visual information recorded from the LGN of animals devoid of photoreceptor cells would be important. However, a comparison of response patterns to photic stimulation between animal

groups was intended to aid in understanding the underlying differences in visual information transfer between the two animal groups.

A total of 525 LGN cells were studied from a total of 23 adult, female albino rats. In seventeen control rats (animals with normal retinas), a total of 365 cells were studied. The remaining 160 LGN cells were studied in six experimental rats with extensive retinal damage. The response patterns of 130 LGN cells from the control animals and 45 LGN cells from the experimental animals were examined with computer analysis techniques (see Table 2). These cells were studied using the PST Histogram Paradigm. In several instances, the Time Interval Histogram was used to investigate the rhythmicity in spontaneous neuronal activity. The cells were classified according to their response patterns generated by flash stimulation. The remaining LGN cells were not fully analyzed due to the low voltage of action potentials or the inability to record the entire sequence of response patterns.

The LGN cells of both experimental and control animals were classified according to their response patterns which could be directly recorded or relayed to the computer for analysis. Fig 6 ("INTACT RETINAS") illustrates an example of the neuronal activity recorded from a cell of the LGN of a control animal. The spontaneous activity

Table 2. Lateral Geniculate Nuclei Cells Studied With Response Patterns

Animal Group	Cell Type	Number of cells
Normal retina:		
	SIMPLE-ON	32
	SIMPLE-OFF	18
	COMPLEX	80
Degenerate retina:		
	COMPLEX	45

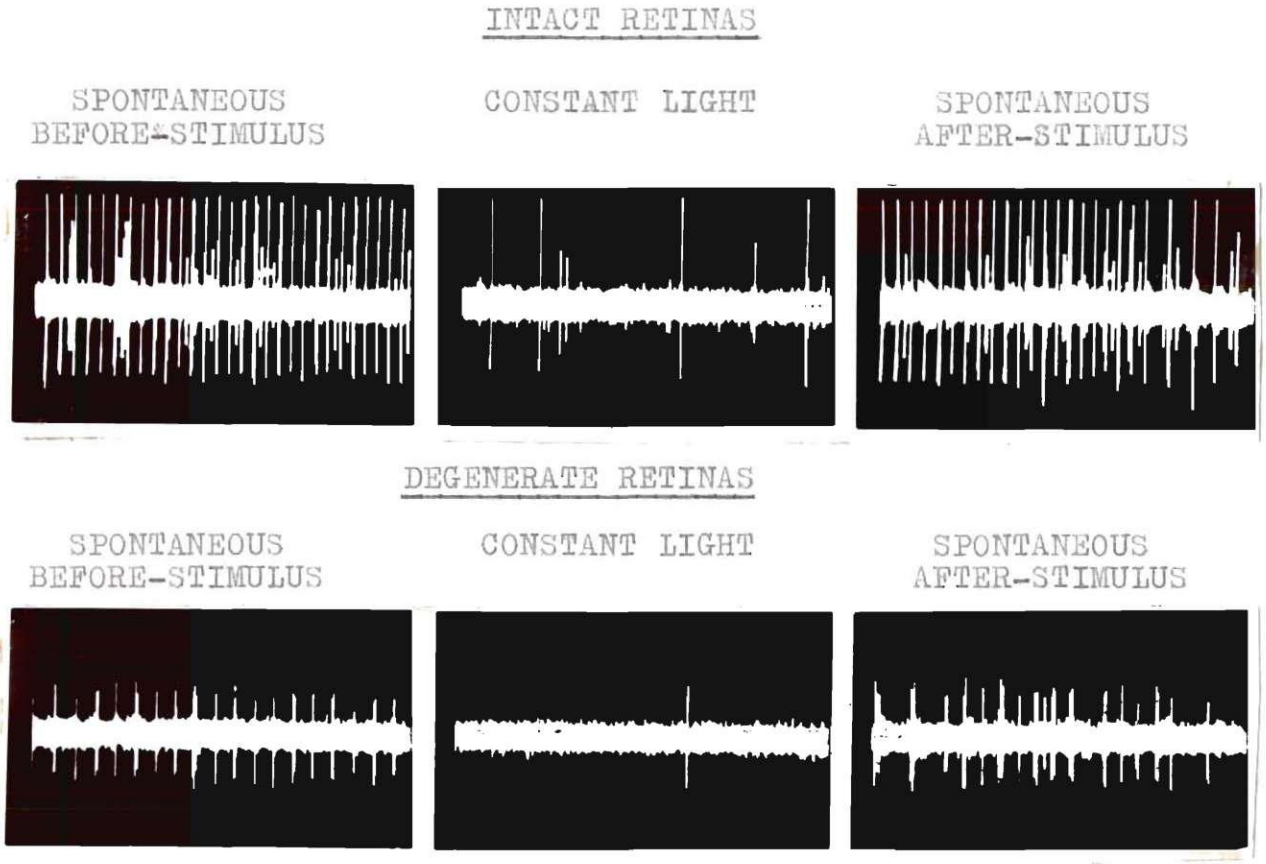


Figure 6. Example of Neuronal Activity Recorded From LGN Cells (Total sweep time 500 msec; maximum amplitude .50 mv)

of the LGN cell in the absence of any visual stimulation is shown in Fig 6 ("SPONTANEOUS BEFORE STIMULUS"). A partial suppression in the rate of activity occurred following an increase in ambient light (Fig 6, "CONSTANT LIGHT"). Following the cessation of the light stimulus, the LGN cell returned to the control level of spontaneous activity (Fig 6, "SPONTANEOUS AFTER STIMULUS"). A similar example of neuronal activity was recorded from a LGN cell of an experimental animal, whose retinas were devoid of photoreceptor cells (Fig 6, "DEGENERATE RETINAS"). The control activity of the LGN cell, in the absence of any visual stimulation is shown in Fig 6 ("SPONTANEOUS PRE-STIMULUS"). When the ambient light was increased, the LGN cell displayed a partial suppression in the rate of neural discharges. Following the cessation of the light stimulus, the LGN cell resumed firing at pre-stimulus levels (Fig 6, "SPONTANEOUS POST-STIMULUS").

The PST histograms illustrate the response activity of neurons to photic stimulation. The sensitivity of LGN neurons to visual stimuli was determined by comparing control Time histograms of spontaneous activity with the PST histograms generated from photic stimulation. Neurons firing spontaneously (no photic stimulation) typically show an envelop of activity best fitted with a straight horizontal line (refer to Chapter III, Fig 4 for discussion of

PST histograms). Therefore, the probability of an action potential occurring during the different time intervals of the histogram would be nearly equal. However, when a neuron is influenced by visual stimulation, the response pattern displays one or more periods of increased excitability. The waves of excitation represent increases in the probability of a neuron firing following visual stimulation. The greater the amplitude of the wave of excitability (highest peaks in the histograms), the greater the probability of an action potential occurring during the excitatory period. The time duration of excitation can range from 10 msec to 2 sec (1-200 BINS). Additionally, the waves of decreased activity indicated intervals of time following stimulation, in which a neuron exhibited a decreased occurrence of action potentials. Thus, the PST histograms express probability-time distributions for the occurrence of action potentials.

Data From Normal Retinal Rats

A comparison of firing properties of LGN cells recorded from control animals (Figs 7-13) resulted in a classification of these cells, according to their response patterns. The effect of light stimulation on the LGN cells varied from producing simple response patterns to evoking very complex patterns of response. While the simple response patterns were not as common as the more complex

patterns, they were the easiest to explain. Figures 7 and 8 illustrate similar simple response patterns of two LGN cells to flashes of light. In these neurons, a single wave of excitation occurred between 20-30 msec (see Fig 7, "FLASH") following stimulation, indicating an elevated probability of firing during this period. The time duration for the period of excitation was relatively constant for each cell, but varied between cells (total range of 20-40 msec). This group of LGN cells exhibit spontaneous rates which vary between 0.1 (see Fig 7, "SPONTANEOUS") and 4.0 discharges/second. Fig 8 is a second example of the simple response pattern to flash stimulation (Fig 8, "FLASH") from another LGN cell. In addition, Fig 8 ("CONSTANT LIGHT + FLASH") illustrates a response pattern evoked by flash stimuli during an increased ambient illumination. In this cell, as is the case for most simple cells, the increased ambient light does not alter the response pattern evoked by the flash stimulation.

The complex response patterns (Figs 9-13) reveal in addition to the short latency (20-30 msec), short duration (10-20 msec) wave of excitation of the simple response patterns, longer latency, longer duration waves of excitation (latencies 60-1800 msec). In all complex neurons, flashes of light evoked responses that are characterized by several periods of increased or decreased excitability.

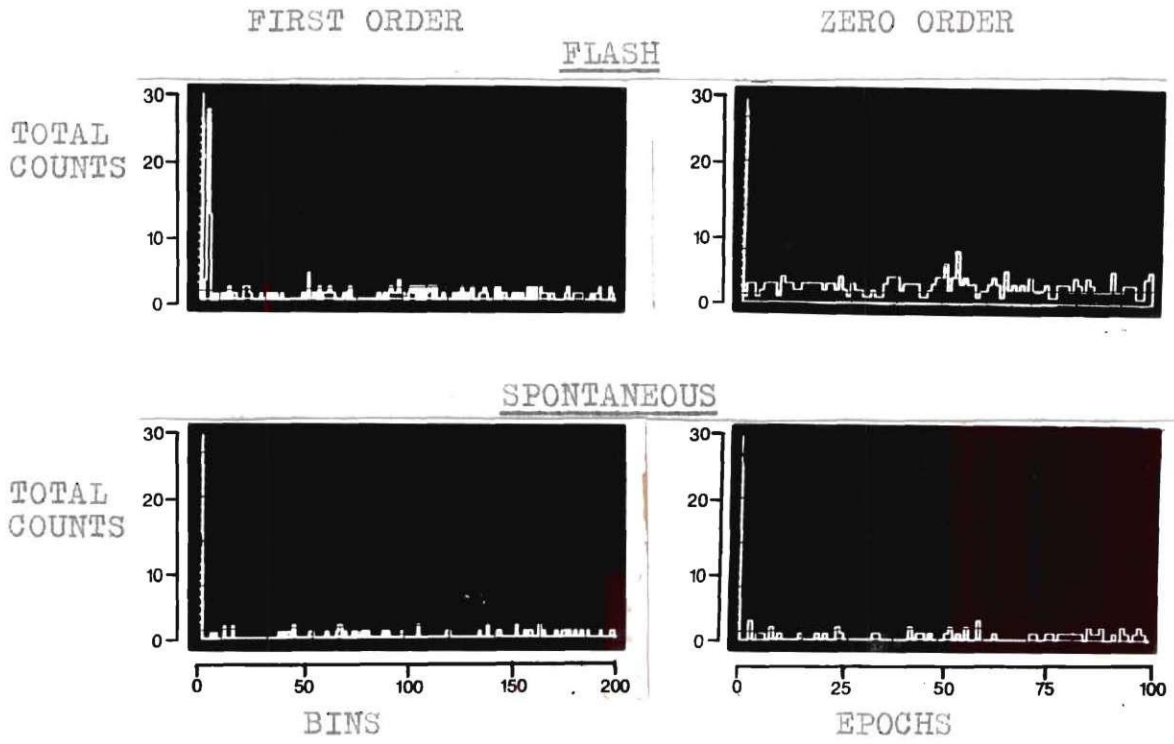


Figure 7. An Example of a Simple Response Pattern

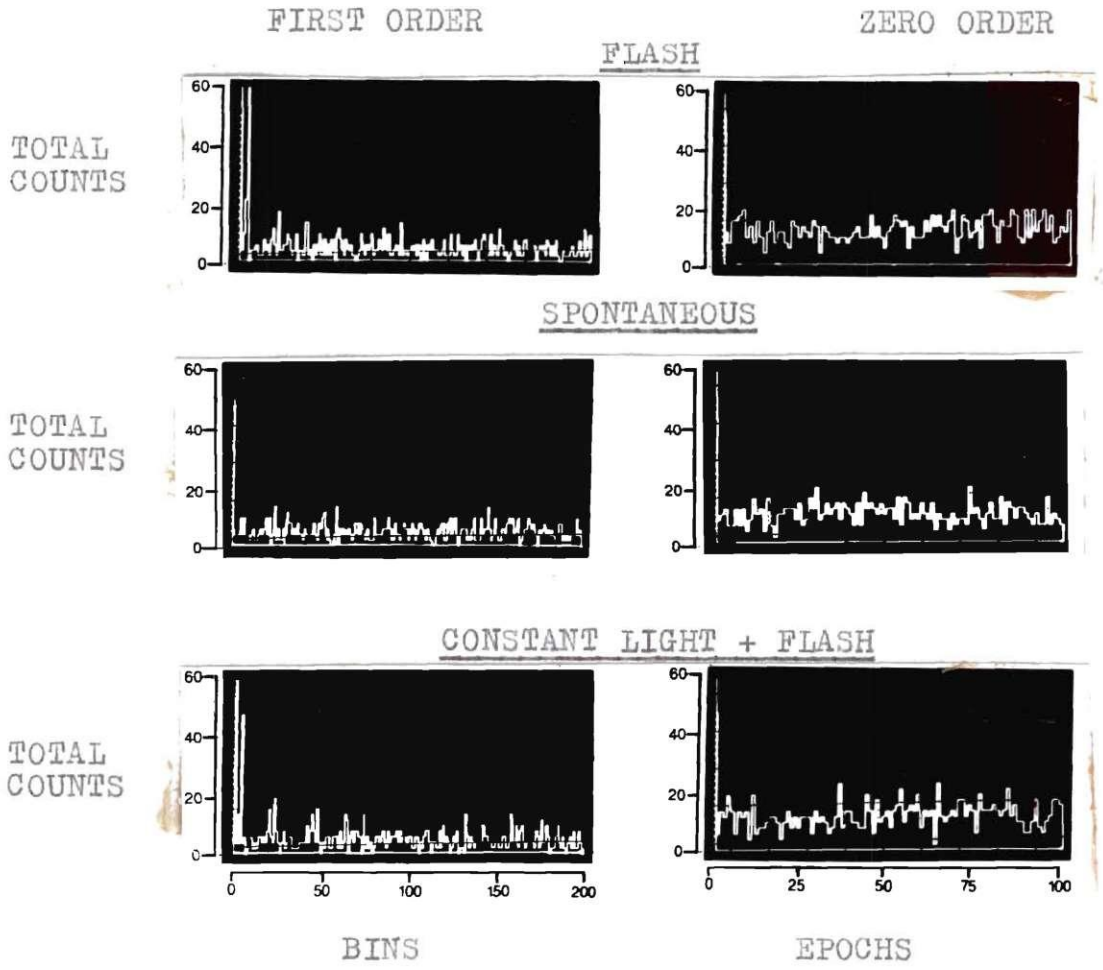


Figure 8. A Simple Response Pattern-Second Example

The duration of the long latency (beyond 250 msec) waves of excitability greatly exceed the short duration waves with early latencies. In most response patterns to flash stimuli, the complex cells reveal short latency waves with greater amplitude than the long latency waves of activity.

The response of a complex neuron showing a single wave of excitation, 10 msec in duration, followed by a prolonged wave of excitability is illustrated in Fig 9 ("FLASH"). A bursting of discharges produced the wave of excitability between 240 and 380 msec (BINS 24-38). A wave of decreased excitability or suppressed activity, 30-200 msec following flash stimulation, is also evident. In most complex cells, the periods of suppression of activity were denoted by spaces in the response pattern and varied in number and duration from one cell to another.

A response pattern evoked by flash stimuli, similar to Fig 9, is illustrated in Fig 10. This neuron exhibited a single wave of excitation (20-30 msec), followed by a wave of decreased excitability (50-220 msec) and a longer latency wave of excitability at a latency of 250-800 msec (see Fig 10, "FLASH"). During an increased ambient lighting (Fig 10, "CONSTANT LIGHT + FLASH"), the short latency wave of excitation was not evoked by the flash stimuli. This finding was observed in most complex cells. However, a comparison of response patterns of Fig 10 ("CONSTANT

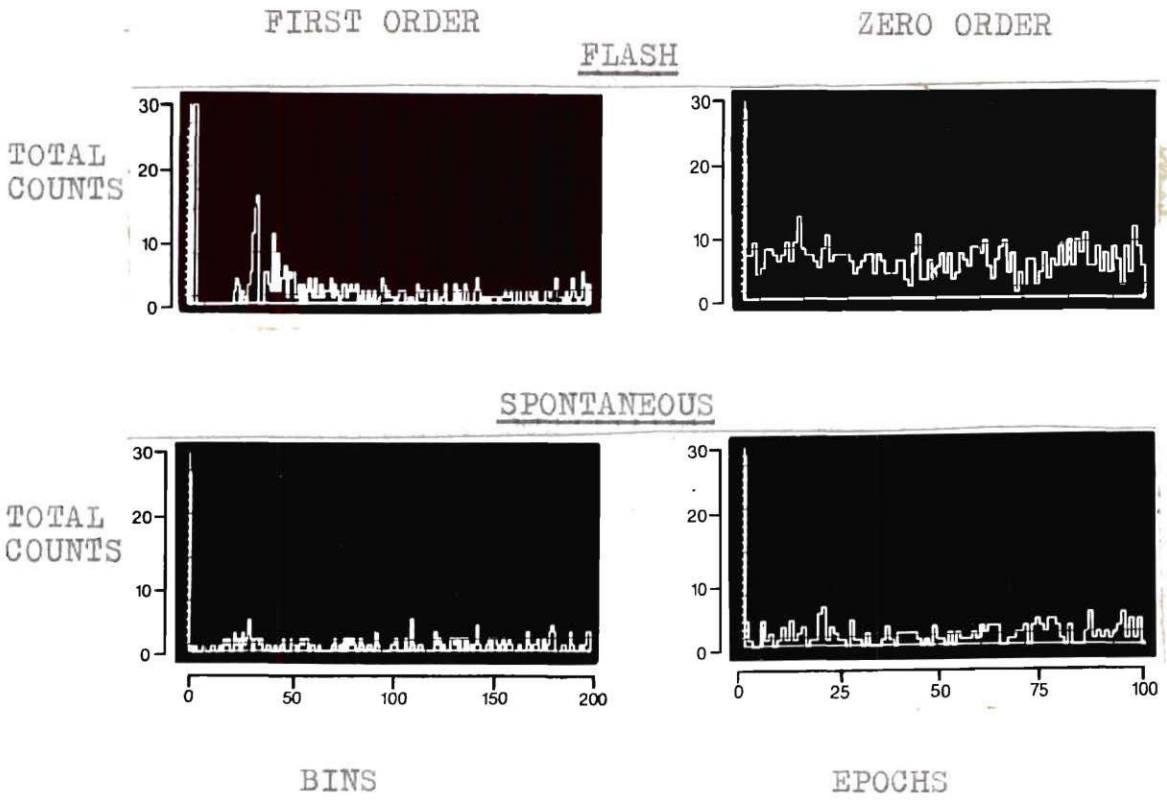


Figure 9. An Example of the Complex Response Pattern

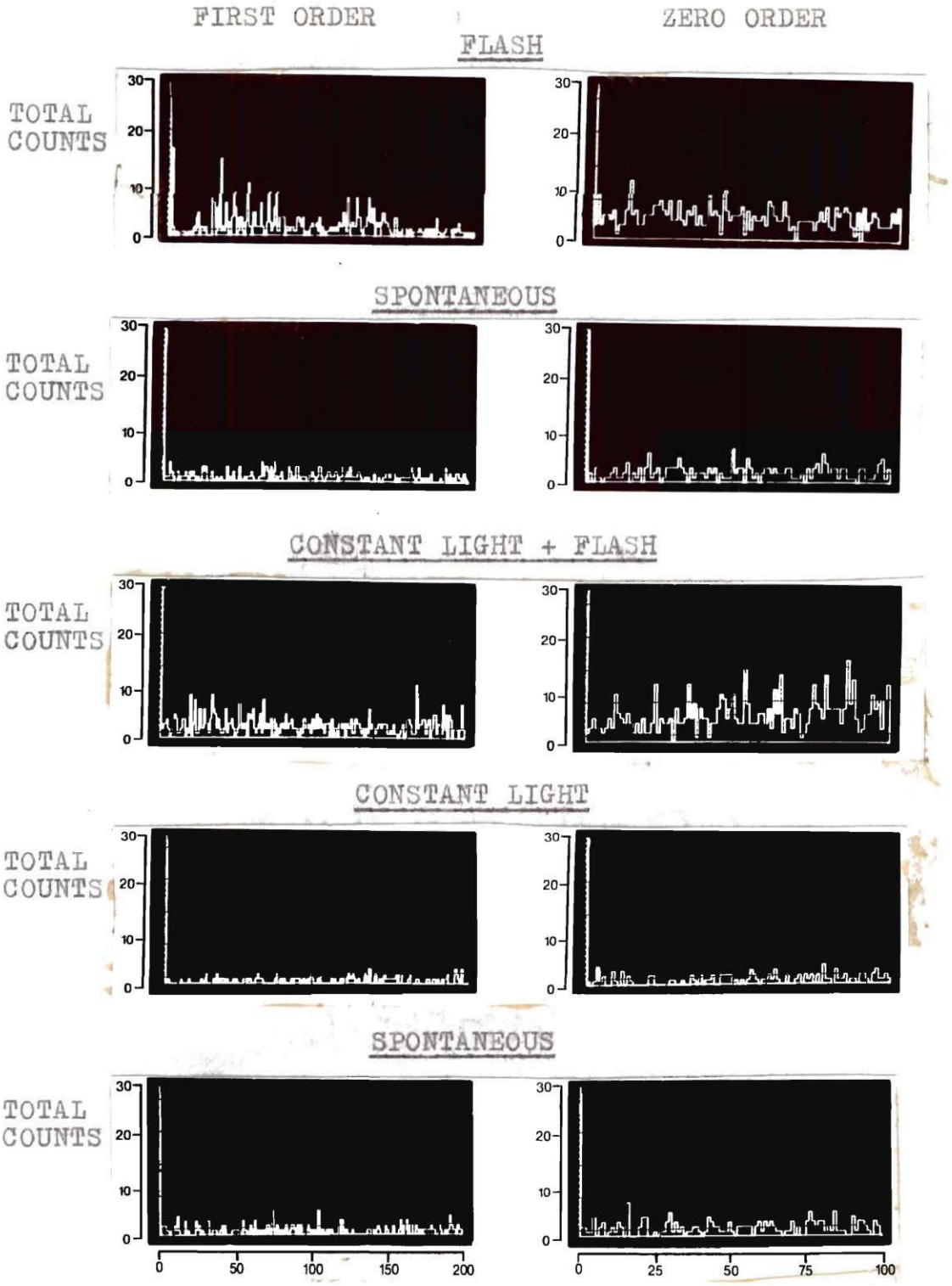


Figure 10. A Complete Response Pattern (Complex)

LIGHT + FLASH" and "CONSTANT LIGHT") reveal the presence of a long duration wave of excitability produced by bursts of discharges evoked by the flash stimuli. Additionally, Fig 10 ("SPONTANEOUS") illustrates a comparable rate of activity prior and after analysis.

Another example of the complexity seen in the response patterns to photic stimulation can be seen in Fig 11. Fig ("FLASH") shows a LGN cell revealing three short duration, short latency (20-30 msec; 200-210 msec; 280-290 msec) waves of excitation evoked by flash stimuli. A long duration wave of excitation at a latency of 310-1400 msec followed the short latency waves of activity. The response pattern produced by the flash stimuli during an increased ambient light (Fig 11, "CONSTANT LIGHT + FLASH") revealed the notable absence of both the short latency and the prolonged waves of excitation evoked by the flash stimulus. A characteristic of some complex cells, after an increase in ambient illumination is the partial suppression of neuronal activity (see Fig 11, "CONSTANT LIGHT"). The time duration for the suppression of action potentials following the onset of the constant light stimuli varied from one cell to another. In most instances, the period of suppressed activity following constant light stimulation did not last beyond 150 seconds after the onset of the light. It was obvious during these experiments that the duration of

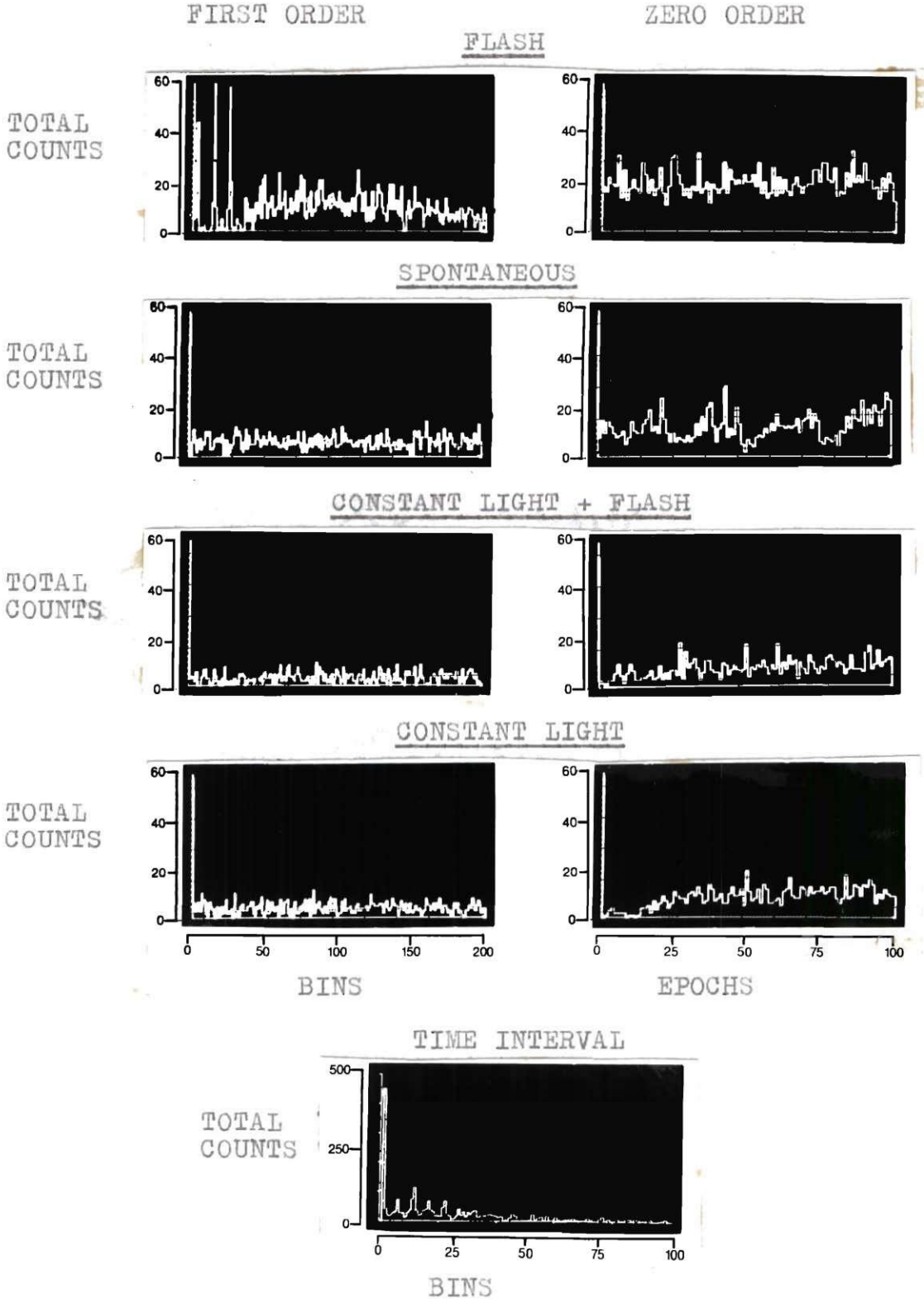


Figure 11. Complex Response Patterns-Prolonged Waves

suppressed activity was dependent upon the level of background illumination, although further analysis of this effect was left for future experimentation.

A suppression in the neuronal activity of some LGN cells can be evoked by the flash stimuli, as illustrated in Fig 12. A wave of decreased excitability evoked by the light, characteristic of all simple-off neurons, occurred between 30 msec and 100 msec (Fig 12, "FLASH"). The peak in the wave of decreased excitability revealed a total suppression of activity between 60-70 msec following the flash stimuli. In the absence of any visual stimulation, these complex cells reveal a high rate of spontaneous activity, approximately 20-30 discharges/second (Fig 12, "SPONTANEOUS").

The complex response patterns of some LGN cells, quite unlike those so far described is illustrated in Fig 13. One of the most unusual response patterns of the complex cells to flash stimulation is illustrated in Fig 13 ("FLASH"). The response pattern displayed a single short latency (20-30 msec) wave of excitation, followed by several longer duration waves of excitability (260-1300 msec). A partial suppression of activity occurred between the waves of excitation. After increasing the ambient light, the evoked response to the flash stimuli (Fig 13, "CONSTANT LIGHT + FLASH") revealed only the short latency wave of

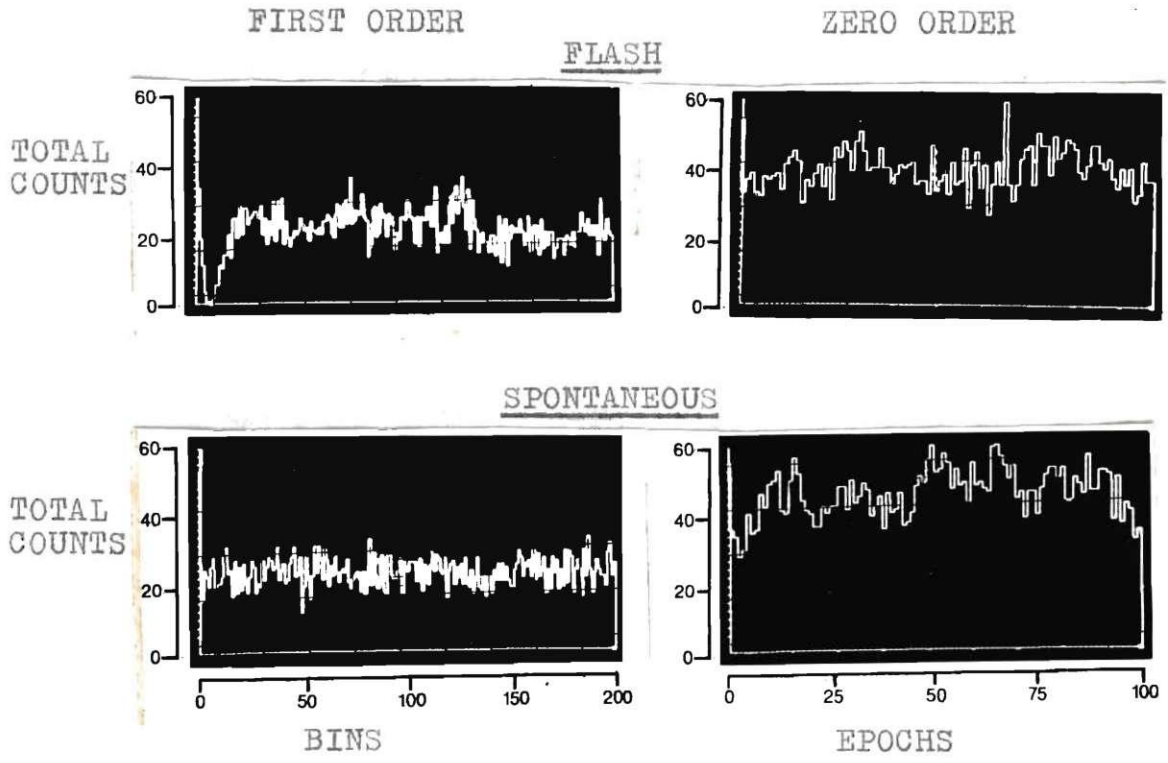


Figure 12. A Simple-Off Response Pattern

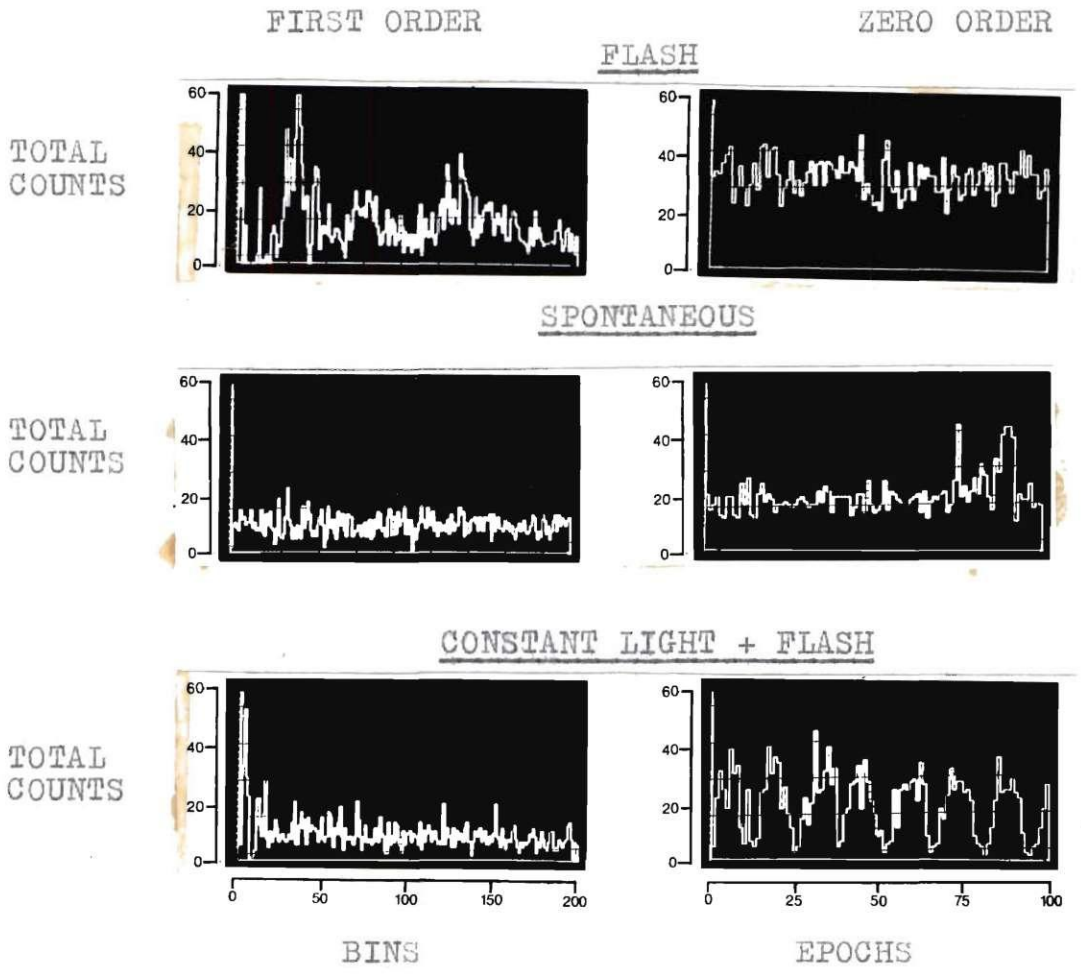


Figure 13. An Unusual Complex Response Pattern

excitation (latency 20-30 msec).

Data from Retinal Damaged Rats

The response patterns of LGN cells from the experimental animals with extensive retinal damage, demonstrate the same complexity as in the control data. The responses of most of the LGN cells to flash stimulation revealed a single short latency wave of excitation, 20 msec in duration. However, the latency of the wave of excitation varied from 70 to 120 msec. A period of complete suppressed activity (wave of decreased excitability) usually followed the wave of increased excitability. The time duration for the suppressed activity was also variable among the cells of the experimental group (total range 150-380 msec). Figures 14 and 15 illustrate examples of the complex nature of these LGN cells. Fig 14 ("FLASH") shows a short duration wave of excitation 100-110 msec after the flash stimuli, indicating a high probability of evoking a response. A complete suppression of neuronal activity followed the wave of excitation. No long latency waves of excitability were evoked by the flash stimuli, a finding observed in most cells of this group. After increasing the ambient illumination the response pattern evoked by the light flashes revealed no periods of increased or decreased activity (Fig 14, "CONSTANT LIGHT + FLASH"). A time interval histogram for the LGN cell's spontaneous activity

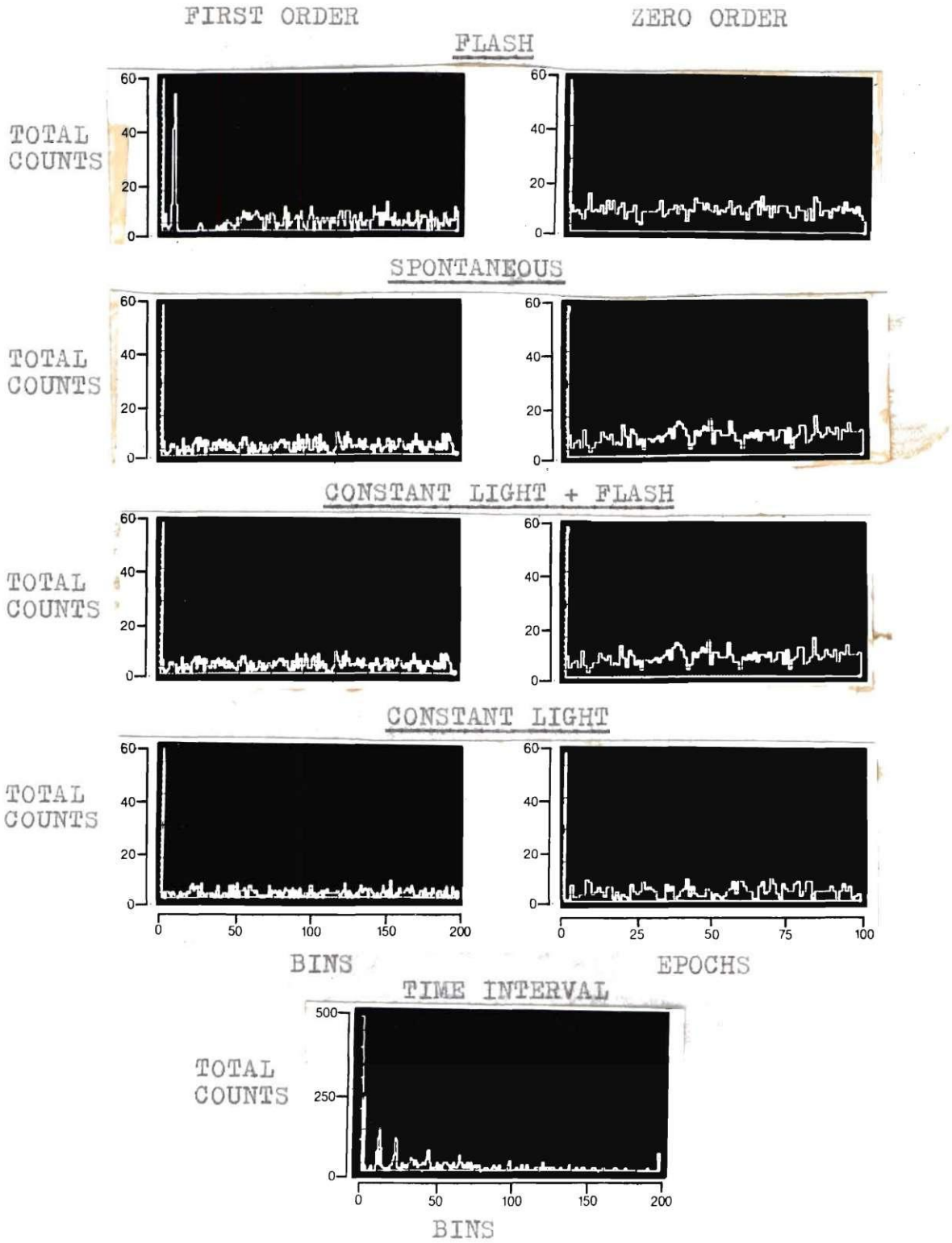


Figure 14. Complex Response Pattern-Degenerate Retinas

revealed a distinct rhythmicity in the rate of neuronal activity (Fig 14, "TIME INTERVAL").

In some LGN cells from the experimental group, the complexity in response patterns made it difficult to ascertain the extent of the evoked response. A widely varying frequency of spontaneous activity causes difficulty in demonstrating the effect of photic stimulation. Fig 15 ("FLASH") illustrates a neuron that appears to exhibit a long latency (230-260 msec) wave of excitation following flash stimulation. Further analysis of the data will be needed to verify the existence of a visual response.

Tissue Examination

Eventually brain tissue from every animal was examined for validation of recording locations. The retinas from the experimental group of animals were compared with the retinas of the control group. There were no observable damaging effects of light on the retinas of control rats exposed for an indefinite time to a cyclic photoperiod of 14 hours of light and 10 hours of darkness (Fig 16, Frame A). After more than 150 days of exposure to continuous low level illumination, no normal, intact photoreceptor cells were observed in any retinal examination from the experimental group (Fig 16, Frame B). The inner nuclear layer appears to be in close proximity to the choriocapillary coat, as the two layers are separated only by a thin zone of glial tissue.

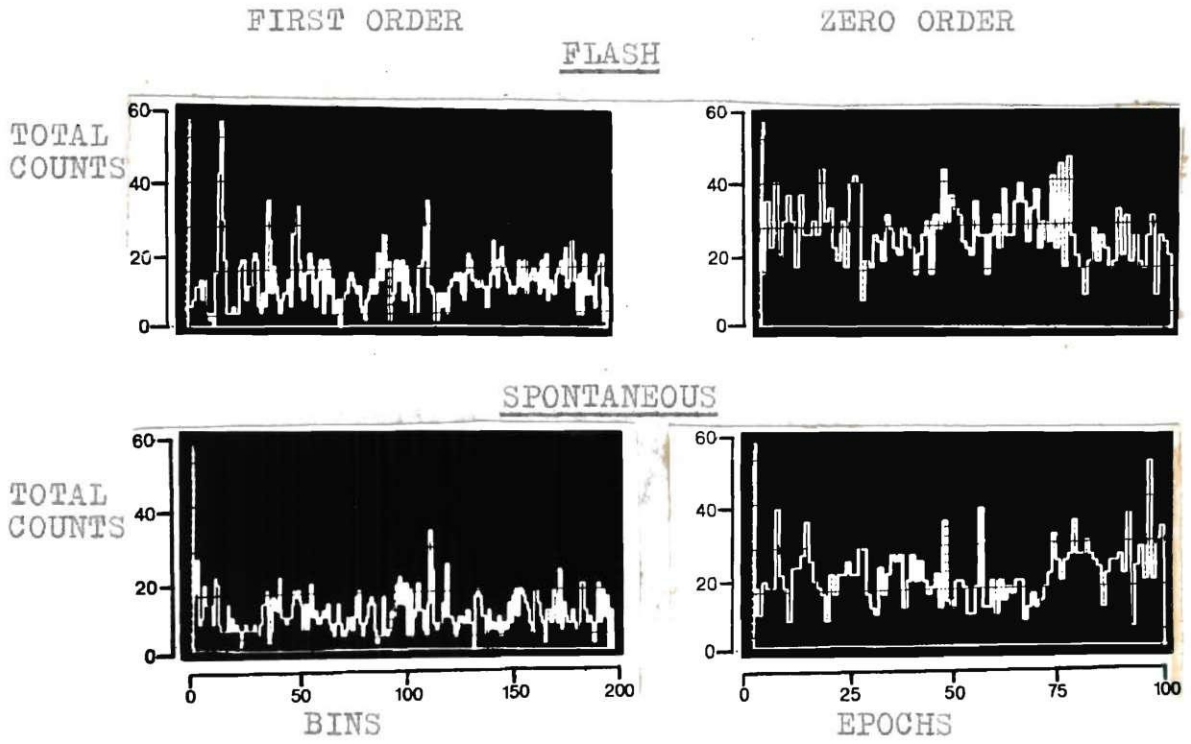


Figure 15. Complex Response Pattern-Degenerate Retinas (A Second Example)

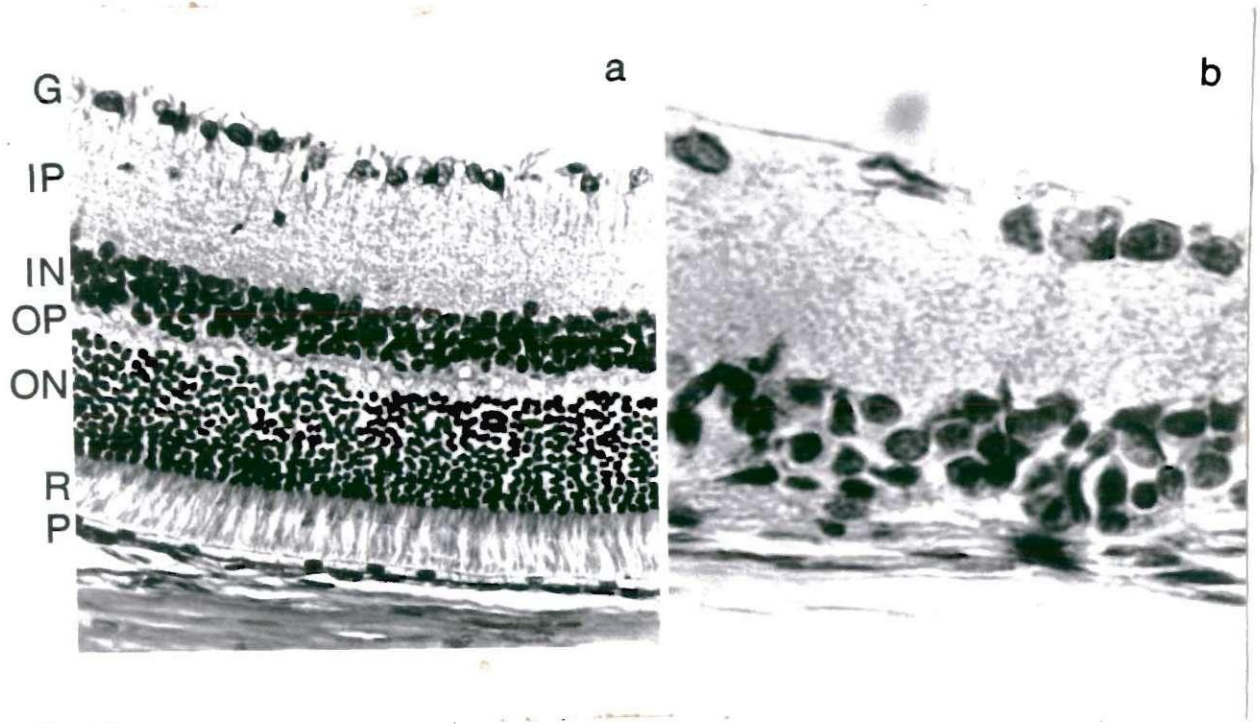


Figure 16. Example of Normal Intact Retina and Retina Devoid of Photoreceptor Cells

Layers of the retina are: G, ganglion; IP, inner plexiform; IN, inner nuclear; OP, outer plexiform; ON, outer nuclear; R, receptor cell; P, pigment epithelium.. (Magnification: a, 400X; b, 1000X)

CHAPTER V

DISCUSSION

This experiment has helped to characterize the response patterns of neurons in the lateral geniculate nucleus (LGN) of control rats with intact retinas and, more importantly, in the LGN of experimental animals with extensive retinal degeneration. The cells of the LGN of both animal groups can be classified according to their responses to visual stimulation of the contralateral retina. The comparison of response patterns indicates that distinctive features of the histograms can differentiate cell types. The distinquishing characteristics of the response pattern histograms include:

(a) a single wave of excitation, 20-30 msec following stimulation, 10 msec duration

(b) a single wave of decreased excitability, 50-80 msec following stimulation

(c) several waves of excitability, varying from 20-1400 msec in duration

(d) long duration (greater than 30 msec) wave of decreased excitability

Neurons from the LGN of animals with normal retinas, can be divided into three distinct categories according to their response pattern to flashes of light. One group of LGN cells respond to a flash of light with a single short

latency (20-30 msec) wave of excitation (SIMPLE-ON GROUP). These cells typically possess a low rate (0.1 to 4.0 discharges/second) of control activity. Another group of cells display a suppression in the neuronal activity following the presentation of a light flash (SIMPLE-OFF GROUP) and usually exhibit high rates of control activity (10-30 discharges/second). However, the largest group of LGN cells studied from the control subjects display far more complex response patterns (COMPLEX GROUP) than those established for the first two cell types. The activity evoked by the light flashes was demonstrated by several waves of excitation and periods of decreased excitability. The largest subgroup of COMPLEX cells show a response pattern evoked by flashes of light characterized by a single short latency (20-30 msec) wave of excitation, followed by a period of complete suppression of neuronal activity and finally a prolonged (long duration) wave of excitability. The response patterns of another group of COMPLEX cells display three short duration (10 msec) waves of excitation followed by a prolonged (300-1400 msec) wave of excitability.

A comparison of the response patterns to various photic stimuli of neurons of the LGN in control animals illustrates the complexity within cell types. In many instances, the response patterns of cells of the SIMPLE-ON

group, evoked by flashes of light during an increased ambient illumination are not necessarily similar. However, most of the SIMPLE-ON cells reveal a short latency wave of excitation to the visual stimulus. The response patterns of cells of the SIMPLE-OFF group do not necessarily reveal a wave of suppressed activity, or decreased excitability, when influenced by light flashes during an increased background illumination. Cells of the COMPLEX group demonstrate a variety of response patterns during an increased ambient illumination. When influenced only by an increased ambient light, some COMPLEX cells exhibit a suppressed rate of activity. This characteristic of many COMPLEX cells varys with respect to time duration and degree of suppression. In some instances, a total suppression of activity was evident 10 msec following stimulation. A gradual increase in the neuronal activity followed the period of suppression. In a few instances, COMPLEX cells display unusual rhythmicity in the number of action potentials evoked by succeeding flashes of light.

A comparison of response patterns of LGN cells from the experimental and control animals was designed to encourage an understanding of the functional difference between the two groups. The response patterns of the LGN cells from the experimental animals, whose retinas were devoid of photoreceptor cells, to flashes of light display features

of the response patterns of the control data COMPLEX cell type. Response patterns of neurons of the experimental group show a single short latency (70 to 120 msec), short duration (10-20 msec) wave of excitation, followed by a supporession of neuronal activity. However, no prolonged, long duration waves of excitation or suppressed activity beyond 230 msec from the stimulus, were evident in the response activity to a flash of light. An obvious similarity between the control and experimental data is the antagonistic effect between the increased ambient illumination and the flashes of light. No waves of excitation were seen when both stimuli were simultaneously presented to the retina. While the similarities in evoked responses suggests a normal functional LGN in animals with retinal damage, the data is not inconsistent with the possibility of an alteration in function.

This experiment, and results from other experimental labs (Kimura, 1962; Fukuda, Sugitani and Iwana, 1973) using photic stimulation of the retina to study visual function, leaves several unresolved questions. It remains unclear why particular cells of the LGN of control animals respond in very complex manners, producing several responses with long latencies to a single flash of light. Conversely, why other LGN cells produce simple response patterns remains unclear. The study of response patterns of LGN cells from

control animals is not nearly complete. Improvement in photic stimulation techniques would allow for greater diversity in presenting visual stimulation. An understanding of the connections within the LGN is eventually necessary (see Chapter 2, LITERATURE REVIEW, Proposed Model of the LGN) to predict cell behavior to complex visual conditions. An equally important question arises as to what retinal elements are necessary to support visual function. A more extensive study of response patterns produced from experimental animals with degenerative retinas is obviously needed to unravel the differences in visual information transfer. The mechanism by which an animal devoid of photoreceptor cells, can perceive visual cues and transmit visual information along the central nervous system is unresolved. The process of transduction within the degenerate retina might also aid in understanding visual informationtransfer in the central nervous system. Although extremely difficult, intracellular recording from the retina of animals with various stages of degeneration could help to understand the process of transduction. Whether this study might assist in understanding information transfer in the mammalian visual system is left for future researchers to resolve. In conclusion, although visual information has been recorded from experimental animals with retinal damage, many questions remain unanswered.

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